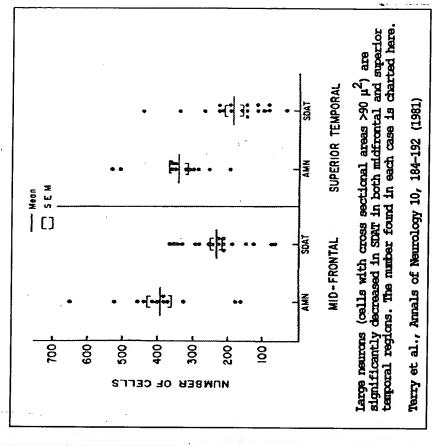
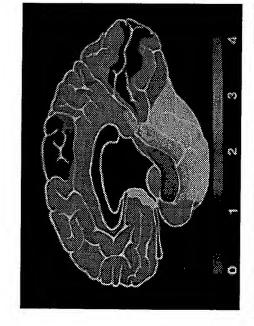
Figure 1

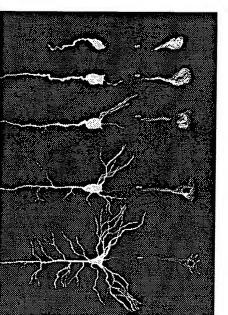
Selective vulnerability of brain regions in Alzheimer's disease

(9)

DSESIZEL IDIEGI







Identification of genes differentially expressed in AD brain regions

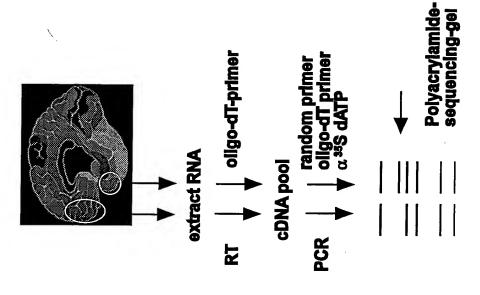
cut out differentially expressed bands

reamplify eluted cDNAs

cloning and sequencing

expression analysis

functional analysis



Identification of genes differentially expressed in AD brain regions

(E)

Material:

AD brain tissue

post mortem time intervall <6h

2 different regions histologically characterized

- inferior temporal lobe

frontal cortex

Method:

mRNA differential display screen

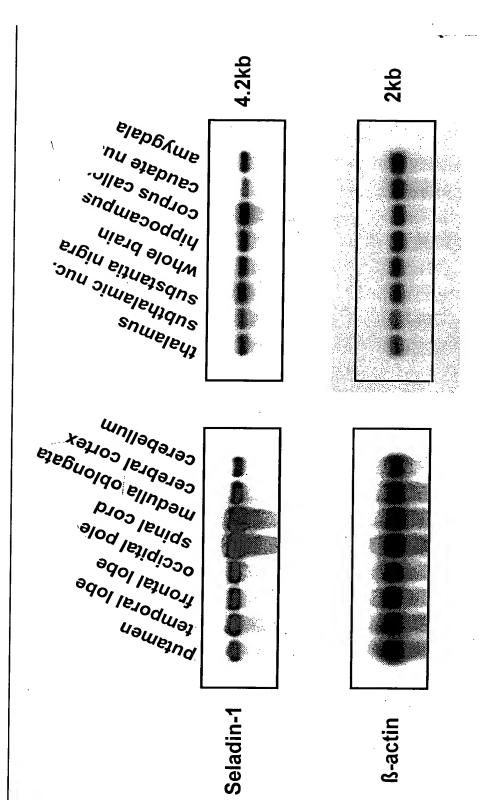
Expression of Seladin-1 in AD brain

(19)

4.2kb 2kb frontal lobe frontal temp. lobe lobe Additional RNA samples from normal (NB) and AD brain NB 2 frontal temp. lobe lobe AD 3 frontal temp. lobe lobe AD 2 RNA samples used for the DD screen frontal frontal temp. lobe lobe lobe AD 1 NB 1 Seladin-1 **ß-actin**

Figure 5

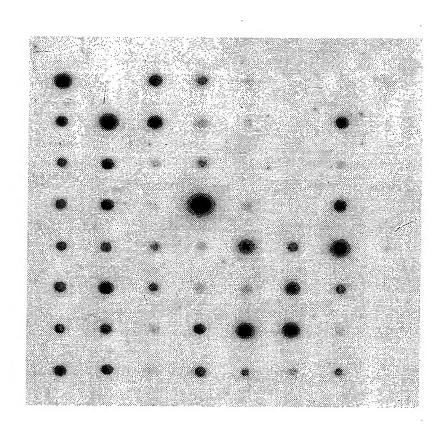
Expression of Seladin-1 in different human brain regions



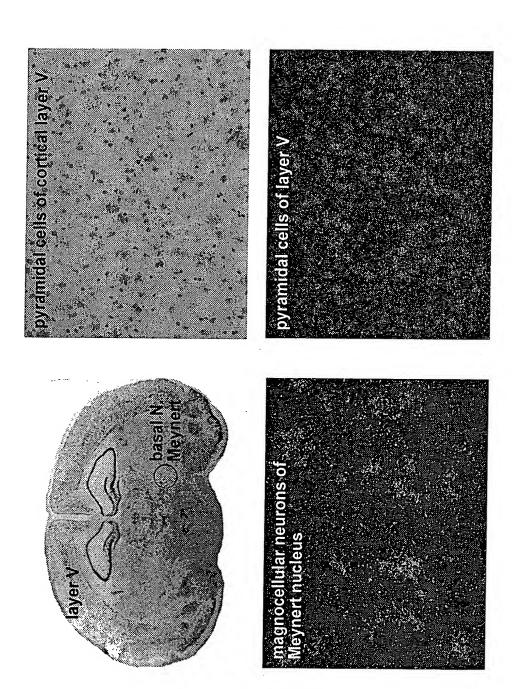
The first party of the party of

Expression of Seladin-1 in human tissues

whole brain	amyg- dala	caudate nucleus	cere- bellum	cerebral cortex	(frontal) (job)	hippo- campus	medulla oblong- ata
occipital lobe	putamen	sub- stantla nigra	(compore) (cho)	thalamus	sub- thalamic nucleus	Spinal)	
heart	aorta	skeletal muscle	colon	bladder	uterus	grasere	stomach
testis	ovary	pancreas	pituitary gland	adrenal gland	thyroid gland	salivary gland	mam- mary gland
kidney	liver	small intestine	ueejds	thymus	periphe- ral leuko- cyte	lymph node	bone
appendix	(ung	trachea	placenta				
fetal brain	fetal heart	fetal kidney	ADAN) (LECT)	(fetal) spleen	fetal thymus	(tetal) (tung)	
yeast total RNA 100ng	yeast tRNA 100ng	E. coli rRNA 100ng	E. coli DNA 100ng	Poly r(A) human Cot1DN 100ng	human Cot1DNA 100ng	human DNA 100ng	human DNA 500ng



Expression of Seladin-1 in rat brain

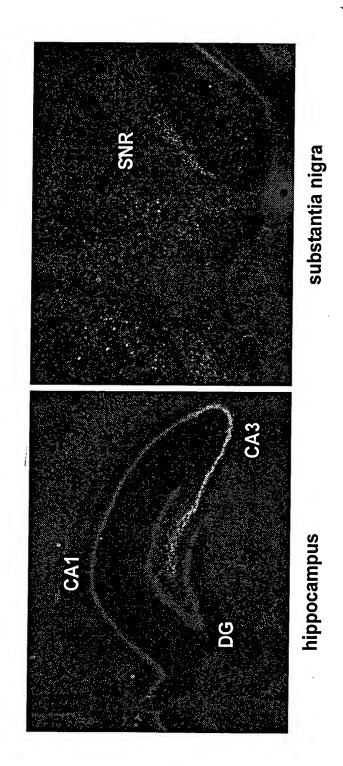


Expression of Seladin-1 in rat brain



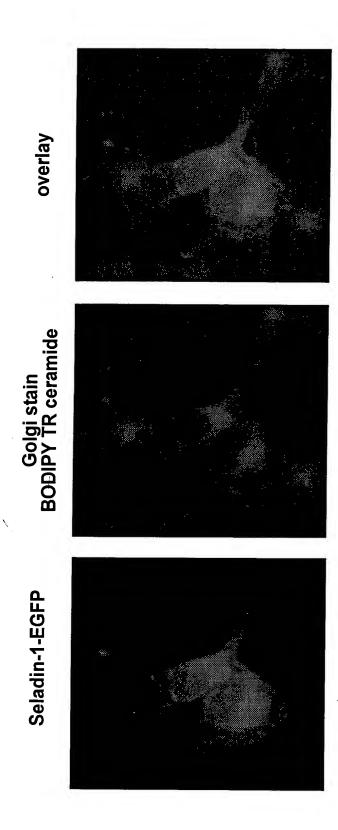
Expression of Seladin-1 in rat brain

(1)



(B)

Subcellular localization of Seladin-1 EGFP fusionprotein



Subcellular localization of Seladin-1

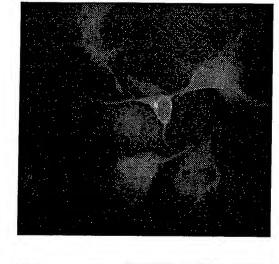
(B)

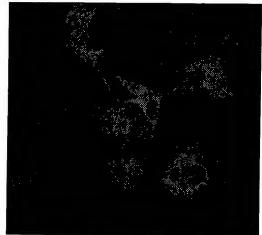
EGFP fusionprotein

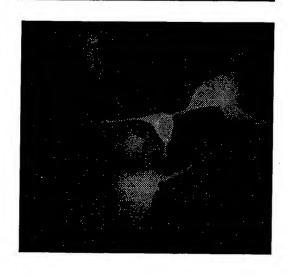
Seladin-1-EGFP

Mitochondrial stain MitoTracker Red CM-H2XRos

overlay





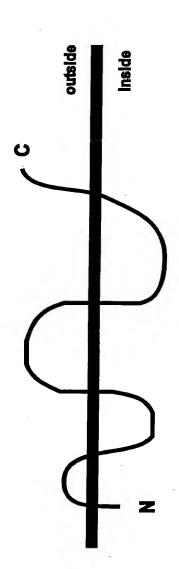


Multiple sequence alignments and secondary structure prediction of Seladin-1

 homology region to many oxido-reductases 516 e.g. L-gulono-gamma-lactone-oxidase 6-hydroxy-d-nicotine oxidase putative mitochondrial targeting sequence **4** ¥

 contains oxygen oxidoreductases covalent FAD binding site

D-lactate dehydrogenase



5 possible transmembrane regions

(E)

- 13 / 29 -

FIGURE 13: SEQ ID NO.1

Seladin-1 amino acid sequence

Seladin-1.orf Length: 516 May 29, 1998 14:51 Type: P Check: 1354 ..

MEPAVSLAVC ALLFLLWVRL KGLEFVLIHQ RWVFVCLFLL PLSLIFDIYY 1 51 YVRAWVVFKL SSAPRLHEQR VRDIQKQVRE WKEQGSKTFM CTGRPGWLTV SLRVGKYKKT HKNIMINLMD ILEVDTKKQI VRVEPLVTMG QVTALLTSIG 101 151 WTLPVLPELD DLTVGGLIMG TGIESSSHKY GLFQHICTAY ELVLADGSFV 201 RCTPSENSDL FYAVPWSCGT LGFLVAAEIR IIPAKKYVKL RFEPVRGLEA 251 ICAKFTHESQ RQENHFVEGL LYSLDEAVIM TGVMTDEAEP SKLNSIGNYY 301 KPWFFKHVEN YLKTNREGLE YIPLRHYYHR HTRSIFWELQ DIIPFGNNPI FRYLFGWMVP PKISLLKLTQ GETLRKLYEQ HHVVQDMLVP MKCLQQALHT 351 401 FQNDIHVYPI WLCPFILPSQ PGLVHPKGNE AELYIDIGAY GEPRVKHFEA RSCMRQLEKF VRSVHGFQML YADCYMNREE FWEMFDGSLY HKLREKLGCQ 451 501 DAFPEVYDKI CKAARH

- 14 / 29 -

FIGURE 14: SEQ ID NO.2 Seladin-1 cDNA sequence

Seladin-1 Length: 4248 April 28, 1998 14:10 Type: N Check: 8184 1 cccgggctgt gggctacagg cgcagagcgg gccaggcgcg gagctggcgg 51 cagtgacagg aggcgcgaac ccgcagcqct taccqcqcqq cqccqcacca tggagcccgc cgtgtcgctg gccgtgtgcg cgctgctctt cctgctgtgg 101 151 gtgcgcctga aggggctgga gttcgtgctc atccaccagc gctgggtgtt 201 cgtgtgcctc ttcctcctgc cgctctcgct tatcttcgat atctactact acgtgcgcgc ctgggtggtg ttcaagctca gcagcgctcc gcgcctgcac 251 301 gagcagcgcg tgcgggacat ccagaagcag gtgcgggaat ggaaggagca 351 gggtagcaag accttcatgt gcacggggcg ccctggctgg ctcactqtct 401 cactacgtgt cgggaagtac aagaagacac acaaaaacat catgatcaac ctgatggaca ttctggaagt ggacaccaag aaacagattg tccgtgtgga 451 501 gcccttggtg accatgggcc aggtgactgc cctgctgacc tccattggct 551 ggactetece egtgttgeet gagettgatg accteaeagt ggggggettg 601 atcatgggca caggcatcga gtcatcatcc cacaagtacg gcctgttcca 651 acacatetge actgettacg agetggteet ggetgatgge agetttgtge gatgcactcc gtccgaaaac tcagacctgt tctatgccgt accctggtcc 701 tgtgggacge tgggtttcct ggtggccgct gagatccgca tcatccctgc 751 801 caagaagtac gtcaagctgc gtttcgagcc agtgcggggc ctggaggcta 851 tctgtgccaa gttcacccac gagtcccagc ggcaggagaa ccacttcgtg 901 gaagggctgc tctactccct ggatgaggct gtcattatga caggggtcat 951 gacagatgag gcagagccca gcaagctgaa tagcattggc aattactaca 1001 agccgtggtt ctttaagcat gtggagaact atctgaagac aaaccgagag 1051 ggcctggagt acattecett gagacactae taccacegee acaegegeag 1101 catcttctgg gagctccagg acatcatccc ctttggcaac aaccccatct 1151 tecgetacet etttggetgg atggtgeete ceaagatete eeteetgaag 1201 ctgacccagg gtgagaccct gcgcaagctg tacgagcagc accacgtggt 1251 gcaggacatg ctggtgccca tgaagtgcct gcagcaggcc ctgcacacct. 1301 tccaaaacga catccacgtc taccccatct ggctgtgtcc gttcatcctg cccagccagc caggcctagt gcaccccaaa ggaaatgagg cagagctcta 1351

- 15 / 29 -

catcgacatt ggagcatatg gggagccgcg tgtgaaacac tttgaagcca 1401 1451 ggtcctgcat gaggcagctg gagaagtttg tccgcagcgt gcatggcttc 1501 cagatgctgt atgccgactg ctacatgaac cgggaggagt tctgggagat 1551 gtttgatggc tccttgtacc acaagctgcg agagaagctg ggttgccagg 1601 acgccttccc cgaggtgtac gacaagatct gcaaggccgc caggcactga 1651 gctggagccc gcctggagag acagacacgt gtgagtggtc aggcatcttc 1701 ccttcactca agcttggctg ctttcctaga tccacacttt caaagagaaa 1751 cccctccaga actcccaccc tgacagccca acaccacctt cctcctggct 1801 tccagggggc agcccagtgg aatggaaaga atgtgggatt tggagtcaga 1851 caageetgag tecagtteee egtttagaae teattagetg tgtgaetetg 1901 ggtgagtccc ttaacccctc tgagcccggg tctcttcatt agttgaaagg 1951 gatagtaata cctacttgca ggttgttgtc atctgagttg agcactggtc 2001 acattgaagg tgctgggtaa gtggtagctc ttgttgcttc ccgttcagcg 2051 tcacatctgc agtggagcct gaaaaggctc cacattaggt cacctgtgca 2101 cagccatggc tggaatgatg aaggggatac gctggagttg ccctgccatc 2151 gcctccatca gccagacgag gtcctcacag gagaaggaca gctcttccc 2201 accetgggat etcaggaggg cagecaegga gtggggagge eccagatgeg 2251 ctgtgccaaa gccaggtccg aggccaaagt tctccctgcc atccttggtg 2301 ccgtcctgcc ccttcctcct tcatgcctgg gcctgcaggc ccaccccagc 2351 caccactgag, tecaetegga gtgeeetgtg tteetggaga aggeatteca 2401 gggttgaatc ttgtcccagc ctcagcctgg gacacctagg tggagagagt 2451 ggtctccgct ctgaattgga tccaggggac ctgggctcat tcttcttggc 2501 tcaccaaccc tgcaggcctc atctttccca aaacccactt tgtcttggtg 2551 ggagtgggtc cgcgctgctc tgcagcaggg gctggggagt ggacagcatc 2601 aggtgggaaa gtggagtcca ccctcatgtt tctgtaggat tctcaccgtg 2651 gggctggaag aaaagagcat cgacttgatt tctccaacca ctcatccctc 2701 tttttctttc ttccaccact ccccacccca gctgtagtta atttcagtgc 2751 cttacaaatc ctaagctcag agaaagttcc atttccgttc cagagggaag 2801 ggaacctccc taggtccttc cctggcttgt tataacgcaa agcttggttg 2851 tttatgcaac tctatcttaa gaactgccca gcctcagctg aaaacccgaa 2901 tctgagaagg aattgcgtca tgtaagggaa gctggaatta agggagctga 2951 gccagtcatg gttgtggcgt gtgagtcagg agacctaggt ttcagccct

- 16 / 29 -

ctctactgtc agcgagctgt gcaacgtggg caagtcattg tcctctgagc 3051 tgcagtttcc tcatctgtca catcgctaca gacaagacct ccctggaacc cttctgattg tcttagacac tgtggttgca aaacccacgg aaagcctcat 3101 3151 ttgtgtggaa agtcagagga aaaatgatcc agtggacact tggggattat 3201 ctgtcattca agatccttcc ttcaacccca aggccagctc ccatctcatt tccagaaagg ctcatacctg gcttgcaggg aagcatctgt cttgtcattc 3251 3301 caggtgccag aatcctctca gagtcattga agggtgttca cccatcccac 3351 ccaaggcttg gcacactgcc agtgtcttag cagggtcttg tgagggctgg 3401 gggcatccag gcactcagaa ggcaaaggaa ccaccctacc catttggcct 3451 ctggagggg cagaagaaag aaagaaacct catcctatat tttacaaagc 3501 atgtgaattc tggcattagc tctcatagga gacccatgtg cttccttgct 3551 cagtgcaaaa ctgatgattc tacttgctgt agatgaatgg ttaacacgag 3601 ctagttaaac agtgccattg ttttgccagt gaagcctcca accctaagcc 3651 actgggacgg tggccagaga tgccagcagc ctctgtcgcc cttagtcata 3701 taaccaaaat ccagacctta tccacaaccc ggggcttgga aaggaaggta 3751 ttttggaatc acaccctccg gttatgttgc tccagtaaaa tcttgcctgg 3801 aaagaggcag tottottagc atggtgagct gagttcatgg cttttttttg 3851 tagccagtcc tgtccctggc catccatgtg atggttttgg atggagttaa 3901 acttgatgcc agtgggcagt gcatgtggaa agtatcagag taagcctctc 3951 ccctccagag\ccctgagttt cttggctgca tgaaggtttt ctttagaatc 4001 agaattgtag ccagtttctt tggccagaag gatgaatact tggatattac 4051 tgaaagggag gggtggagat gggtgtggca gtgtatggtg tgtgattttt 4101 attttcttct ttggtcatgg gggccaagga gaaaggcatg aatcttccct 4151 gtcaggctct tacagccaca ggcactgtgt ctactgtctg gaagacatgt 4201 ccccgtggct gtggggccgc tgcttctgtt taaataaaag tggcctgg

- 17 / 29 -

FIGURE 15 CDNA sequence comparison . KIAA0018/Seladin-1

1	ggcgcgaacccgcagcgcttaccgcgcgcgcgccgcaccatggagcccgcc	50
62		111
51		100
112		161
101		150
162		211
151	tcctcctgcgctctcgcttatcttcgatatctactactacgtgcgcgcc	200
212	tecteetgeegetetegettatettegatatetaetaetaegtgegege	261
201	tgggtggtgttcaagctcagcagcgctccgcgcctgcacgagcagcgcgt	250
262	tgggtggtgttcaagctcagcagcgctccgcgcctgcacgagcagcgcgt	311
251	gcgggacatccagaagcaggtgcgggaatggaaggagcagggtagcaaga	300
312	gcgggacatccagaagcaggtgcgggaatggaaggagcagggtagcaaga	361
301	ccttcatgtgcacggggcgcctggctggctcactgtctcactacgtgtc	350
362	ccttcatgtgcacggggcgccctggctgactgtctcactacgtgtc	411
351	gggaagtacaagaagacacaaaaaacatcatgatcaacctgatggacat	400
412	gggaagtacaagaagacacaaaaaacatcatgatcaacctgatggacat	461
401	tctggaagtggacaccaagaaacagattgtccgtgtggagcccttggtga	450
462	tctggaagtggacaccaagaaacagattgtccgtgtggagcccttggtga	511
451	ccatgggccaggtgactgccctgctgacctccattggctggactctcccc	500
512	ccatgggcaggtgactgcctgctgacctccattggctggactctccc	561
501	gtgttgcctgagcttgatgacctcacagtggggggcttgatcatgggcac	550
562	gtgttgcctgagcttgatgacctcacagtggggggcttgatcatgggcac	611
551	aggcatcgagtcatcatcccacaagtacggcctgttccaacacatctgca	600
612	A A A A A A A A A A A A A A A A A A A	661
601	ctgcttacgagctggtcctggctgatggcagctttgtgcgatgcactccg	650
662		711
551	tccgaaaactcagacctgttctatgccgtaccctggtcctgtgggacgct	700
712		761 .
701	gggtttcctggtggccgctgagatccgcatcatccctgccaagaagtacg	750
62	gggtttcctggtggccgctgagatccgcatcatccctgccaaqaagtacg	811

- 18 / 29 -

75	1 tcaagctgcgtttcgagccagtgcggggcctggaggctatctgtgccaag	800
812		861
803	l ttcacccacgagtcccagcggcaggagaaccacttcgtggaagggctgct	850
862		911
851	ctactccctggatgaggctgtcattatgacaggggtcatgacagatgagg	900
912		961
901		950
962		1011
951		1000
1012		1061
1001	cattcccttgagacactactaccaccgccacacgcgcagcatcttctggg	1050
1062		1111
1051		1100
1112		1161
1101	tttggctggatggtgcctcccaagatctccctcctgaagctgacccaggg	1150
1162		1211
1151	tgagaccctgcgcaag.tgtacgagcagcaccacgtggtgcaggacatgc	1199
1212		1261
1200	tggtgccca tga agtgcctgcagcaggccctgcacaccttccaaaacgac	1249
1262		1311
1250	atccacgtctaccccatctggctgtgtccgttcatcctgcccagccag	1299
1312		1361
1300	aggcctagtgcaccccaaaggaaatgaggcagagctctacatcgacattg	1349
1362		1411
1350	gagcatatggggagccgcgtgtgaaacactttgaagccaggtcctgcatg, 1	1399
1412		461
1400	aggcagctggagaagtttgtccgcagcgtgcatggcttccagatgctgta 1	449
1462	aggcagctggagaagtttgtccgcagcgtgcatggcttccagatgctgta 1	511
1450	tgccgactgctacatgaaccgggaggagttctgggagatgtttgatggct 1	499
1512		561
1500	ccttgtaccacaagctgcgagagaagctgggttgccaggacgccttcccc 1	549
1562		611

1550	gaggtgtacgacaagatctgcaaggccgccaggcactgagctggagcccg	159 9
1612		1661
1600	cctggagagacagacacgtgtgagtggtcaggcatcttcccttcactcaa	1649
1662	cctggagagacagacacgtgtgagtggtcaggcatcttcccttcactcaa	1711
1650	gettggetgettteetagateeacaettteaaagagaaaceeeteeagaa	1699
1712		1761
	ctcccaccctgacagcccaacaccaccttcctcctggcttccagggggca	1749
1762	ctcccacctgacagcccaacaccaccttcctcctggcttccagggggca	1811
1750	-	1799
1812	·	1861
1800	ccagttccccgtttagaactcattagctgtgtgactctgggtgagtccct	1849
1862	ccagttccccgtttagaactcattagctgtgtgactctgggtgagtccct	1911
1850	taacccctctgagcccgggtctcttcattagttgaaagggatagtaatac	1899
1912	taacccctctgagcccgggtctcttcattagttgaaagggatagtaatac	1961
	ctacttgcaggttgttgtcatctgagttgagcactggtcacattgaaggt	1949
1950	gctgggtaagtggtagctcttgttgcttcccgttcagcgtcacatctgca	2011
2012		2061
2000	gtggagcctgaaaaggctccacattaggtcacctgtgcacagccatggct	2049
2062		2111
2050	ggaatgatgaaggggatacgctggagttgccctgccatcgcctccatcag	2099
2112	ggaatgatgaaggggatacgctggagttgccctgccatcgcctccatcag	2161
2100	ccagacgaggtcctcacaggagaaggacagctcttccccaccctgggatc	2149
2162	ccagacgaggtcctcacaggagaaggacagctcttccccacctgggatc	2211
2150	tcaggagggcagccacggagtggggaggcccagatgcgctgtgccaaag	2199
2212	tcaggagggcagccacggagtggggaggccccagatgcgctgtgccaaag	2261
		2249
	ccaggtccgaggccaaagttctccctgccatccttggtgccgtcctgccc	2311
		2299
	cttcctccttcatgcctgggcctgcaggcccaccccagccaccactgagt	2361
		2349
.502	ccactcggagtgccctgtgttcctggagaaggcattccagggttgaatct	2411

- 20 / 29 -

	tgtcccagcctcagcctgggacacctaggtggagagagtggtctccgctc	
2412		246
2400	tgaattggatccaggggacctgggctcattcttcttggctcaccaaccct ()	244
2462		251
2450	gcaggcctcatctttcccaaaacccactttgtcttggtgggagtgggtcc	249
2512		256
2500) gcgctgctctgcagcaggggctggggagtggacagcatcaggtgggaaag	2549
2562		261
2550		2599
2612		2661
2600		2649
2662		2711
2650		2699
2712		2761
2,700		2749
2762		2811
2750	aggtccttccctggcttgttataacgcaaagcttggttgtttatgcaact	2799
2812		2861
2800		2849
2862		2911
2850	attgcgtcatgtaagggaagctggaattaagggagctgagccagtcatgg	2899
2912		2961
2900	ttgtggcgtgtgagtcaggagacctaggtttcagcccctctctactgtca	2949
2962		3011
2950		2999
3012		3061
3000		3049
3062		3111
3050	. cttagacactgtggttgcaaaacccacggaaagcctcatttgtgtggaaa	3099
3112		3161
3100	gtcagaggaaaaatgatccagtggacacttggggattatctgtcattcaa	3149
3162		3211

- 21 / 29 -

3150	gateetteetteaaccccaaggccageteccateteatttecagaaagge	3199
3212	gateetteetteaaceceaaggecageteecateteatttecagaaagge	3261
3200	tcatacctggcttgcagggaagcatctgtcttgtcattccaggtgccaga	3249
3262		3311
3250	atcctctcagagtcattgaagggtgttcacccatcccaccca	3299
3312	atcctctcagagtcattgaagggtgttcacccatcccaccca	3361
3300	cacactgccagtgtcttagcagggtcttgtgagggctggggggcatccagg	3349
3362		3411
3350		3399
3412	cactcagaaggcaaaggaaccaccctacccatttggcctctggaggggc	3461
3400		3449
3462		3511
3450		3499
3512		3561
3500		3549
3562		3611
3550		3599
3612		3661
3600 3662		3649
3650		3711
3712		3699
3700		3761
3762		3749
3750		3811 3799
3812		3861
		3849
3862		
3850		3899
3912		3961.
3900		3949
3962		



- 22 / 29 -

3950	cagtttctttggccagaaggatgaatacttggatattactgaaagggagg	399 9	
4012	cagtttctttggccagaaggatgaatacttggatattactgaaagggagg	4061	
4000	ggtggagatgggtgtggcagtgtatggtgtgtgatttttatttcttctt	4049	
4062	ggtggagatgggtgtggcagtgtatggtgtgtgatttttatttcttctt	4111	
4050	tggtcatgggggccaaggagaaaggcatgaatcttccctgtcaggctctt	4099	
4112	tggtcatgggggccaaggagaaaggcatgaatcttccctgtcaggctctt	4161	
4100	acagccacaggcactgtgtctactgtctggaagacatgtccccgtggctg	4149	
4162	${\tt acagccacaggcactgtgtctactgtctggaagacatgtcccgtggctg}$	4211	
4150	tggggccgctgcttctgtttaaataaaagtggcctgg 4186		
4212	tggggccgctgcttctgtttaaataaaagtggcctgg 4248		

Fig. 16

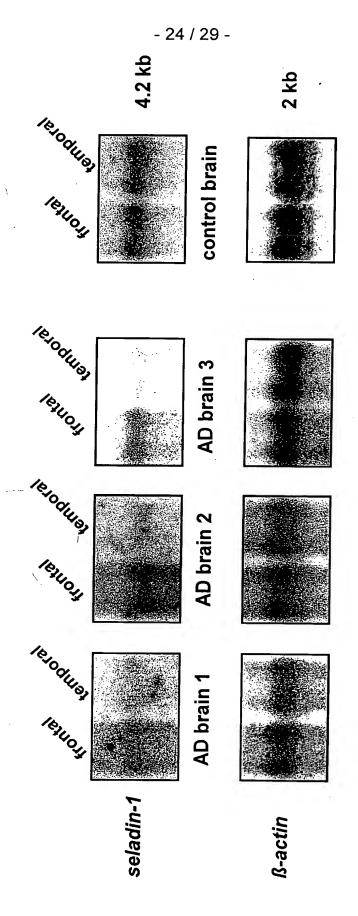


Fig. 17 A

Fig. 17 B

(1)

- 26 / 29 -

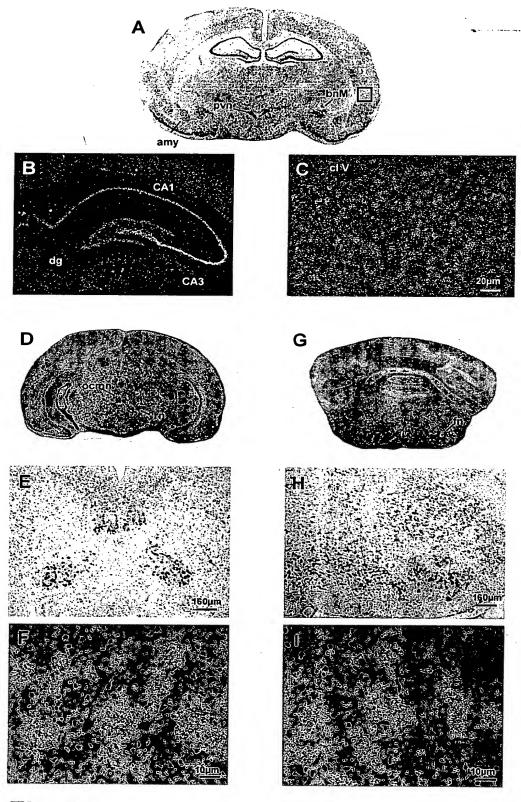


Fig. 18

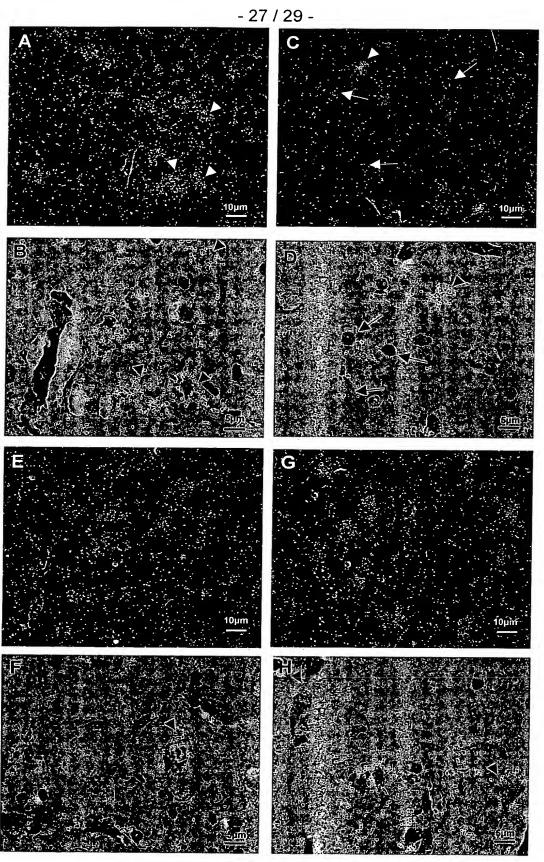


Fig. 19

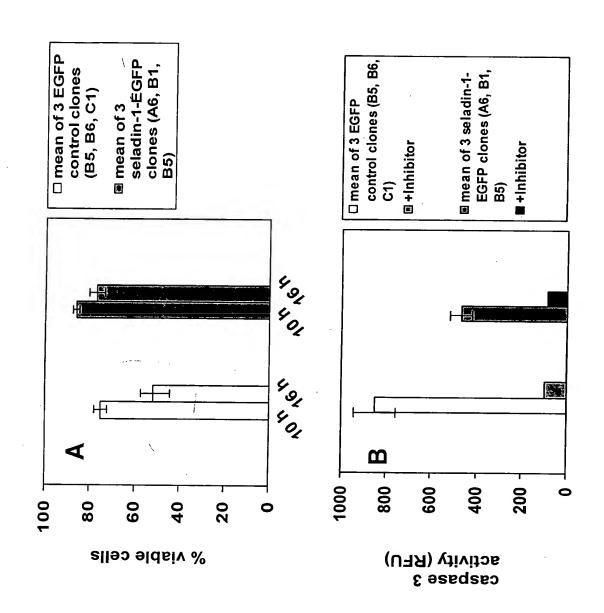


Fig. 20

(19)

49)

Fig. 21